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Proposed Registration Decision PRD2018-11

Tributyl Tetradecyl Phosphonium Chloride and Bellacide 350

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Overview

Proposed Registration Decision for Tributyl Tetradecyl Phosphonium Chloride

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the Pest Control Products Act and Regulations, is proposing registration for the sale and use of Bellacide 350 Technical and Bellacide 350, containing the technical grade active ingredient tributyl tetradecyl phosphonium chloride (TTPC), to control microbial slime formation in enhanced oil recovery systems and fracturing fluid systems.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products is acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Bellacide 350 Technical and Bellacide 350.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides section of Canada.ca.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "... the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on tributyl tetradecyl phosphonium chloride and Bellacide 350, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on tributyl tetradecyl phosphonium chloride and Bellacide 350, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Tributyl Tetradecyl Phosphonium Chloride?

Tributyl tetradecyl phosphonium chloride is an antimicrobial biocide that is effective at preventing microbial slime from forming in oilfield sites such as fracturing fluids and water flooding operations. Tributyl tetradecyl phosphonium chloride acts on cell membranes by making them more permeable and causing important cell components to leak out, ultimately leading to death of the bacteria.

Health Considerations

Can Approved Uses of Tributyl Tetradecyl Phosphonium Chloride Affect Human Health?

Bellacide 350, containing tributyl tetradecyl phosphonium chloride, is unlikely to affect your health when used according to label directions.

Potential exposure to tributyl tetradecyl phosphonium chloride may occur when handling and applying the end-use product, Bellacide 350, or when re-entering treatment sites to conduct clean-up and equipment maintenance. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose level where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

In laboratory animals, both Bellacide 350 Technical, and the end-use product, Bellacide 350, were considered moderately toxic via the oral route and of low toxicity via the dermal route of exposure. They did not cause an allergic skin reaction. Bellacide 350 Technical and Bellacide 350 were considered highly acutely toxic via the inhalation route and corrosive to the eyes and skin. Consequently, the signal words and hazard statements "DANGER POISON" and "CORROSIVE TO EYES AND SKIN" are required on the labels of Bellacide 350 Technical and Bellacide 350.

In the available toxicology studies, there was no evidence to suggest that tributyl tetradecyl phosphonium chloride damaged genetic material. Health effects in animals given repeated oral doses of tributyl tetradecyl phosphonium chloride included clinical signs and reduced body weight. When tributyl tetradecyl phosphonium chloride was given to pregnant animals, effects on the developing fetus were observed at a dose level that also caused toxic effects in the mother, indicating that the young do not appear to be more sensitive to tributyl tetradecyl phosphonium chloride than the adult animal.

It was not possible to fully characterize the potential human health effects of tributyl tetradecyl phosphonium chloride due to the limited available toxicology database. However, exposure to tributyl tetradecyl phosphonium chloride in enhanced oil recovery systems and fracturing fluid systems was determined to be limited. For this reason, no additional toxicology studies were required for the current assessment.

Risks in Residential and Other Non-Occupational Environments

Risks from non-occupational exposure to Bellacide 350 are not expected.

Bystander exposure to Bellacide 350 is not expected to be greater than the exposure to mixer/loader/applicator or postapplication workers.

Occupational Risks From Handling Bellacide 350

Occupational risks are not of concern when Bellacide 350 is used according to the proposed label directions, which include protective measures.

Risks to individuals handling and re-entering areas containing Bellacide 350 are not of concern when the product is used according to label directions.

Applicators (mixing, loading and applying Bellacide 350) can come in direct contact with Bellacide 350 on the skin or through inhalation. Therefore the label will specify that Bellacide 350 must be applied using closed metred systems only (i.e., dry coupling) and anyone mixing, loading, or applying Bellacide 350 must wear coveralls worn over long-sleeved shirt and long pants, socks, chemical-resistant footwear, chemical resistant gloves, and protective eyewear (goggles or face mask).

There is potential for inhalation exposure to workers entering areas containing Bellacide 350. However, no risk of concern is expected for those workers when the product is used according to label directions.

Environmental Considerations

What Happens When Tributyl Tetradecyl Phosphonium Chloride Is Introduced Into the Environment?

Tributyl tetradecyl phosphonium chloride (TTPC) is used as a biocide to prevent and/or inhibit microbial growth and may be mixed with other biocides to increase their effectiveness. When used according to label directions as a biocide in fracturing fluids and well injection waters, tributyl tetradecyl phosphonium chloride does not pose a risk to the environment.

Tributyl tetradecyl phosphonium chloride can enter the environment when used in fracturing fluids, for waterflooding, or during disposal after the fluid has been used underground. Fracturing fluids are a chemical mixture used in oil and gas drilling operations to increase the quantity of hydrocarbons that can be extracted from reservoirs underground. Waterflooding (enhanced oil recovery) is a technical procedure where water and other chemicals, including biocides, are injected into the ground to displace residual oil. For post-use disposal, TTPC may be released unintentionally to soil or water after use as a fracturing fluid or in waterflooding if a waste disposal pipeline is damaged.

If TTPC reaches soil, it will bind to soil and initially resist breakdown by soil micro-organisms. As a result of this behaviour, TTPC is not expected to move downward through soil and reach groundwater. Due to its physical/chemical properties, if TTPC reaches water it will mix readily but is also expected to bind to sediment and other solid particles in water. After it binds to soil or sediment particles, it is expected to break down into several transformation products which may be released back into the overlying water. Because of its chemical properties, TTPC is not expected to be found in air or accumulate in organisms.

TTPC presents a negligible risk to birds and aquatic organisms. At high doses TTPC can be toxic to birds and aquatic organisms but due to its use pattern, the potential exposure of these organisms is expected to be minimal and, consequently, risk to these organisms is not of concern.

Value Considerations

What Is the Value of Bellacide 350?

Bellacide 350 controls microbial slime formation in oilfield operations such as fracturing and waterflooding.

Bellacide 350 provides effective control of microbial slimes in fracturing fluids and in the water used for enhanced oil recovery. It is compatible with current slime-management practices in oilfield operations. The availability of Bellacide 350 in Canada provides a new active ingredient with which to control bacteria that cause problematic biofilms and oil souring. It provides a valuable alternative biocide to an industry where a variety of biocides may be needed to address the microbial problems due to the inherent variation of the different oilfield sites.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Bellacide 350 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

- To avoid direct contact with Bellacide 350 on the skin, the product must be applied using closed metered systems only (i.e., dry coupling). In addition, anyone handling (mixing, loading, or applying) Bellacide 350 must wear coveralls worn over long-sleeved shirt and long pants, socks, chemical-resistant footwear, chemical resistant gloves, and protective eyewear (goggles or face mask).

Environment

- Environmental hazard statements for aquatic organisms are required.

Next Steps

Before making a final registration decision on tributyl tetradecyl phosphonium chloride and Bellacide 350, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the PMRA's response to these comments.

Other Information

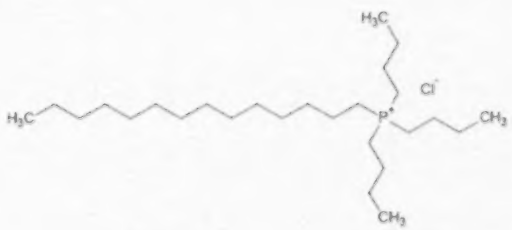
When the PMRA makes its registration decision, it will publish a Registration Decision on tributyl tetradecyl phosphonium chloride and Bellacide 350 (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Tributyl Tetradecyl Phosphonium Chloride

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Tributyl tetradecyl phosphonium chloride
Function	Microbiocide
Chemical name	
1. **International Union of Pure and Applied Chemistry (IUPAC)**	Tributyltetradecylphosphonium chloride
2. **Chemical Abstracts Service (CAS)**	Phosphonium, tributyltetradecyl-, chloride (1:1)
CAS number	81741-28-8
Molecular formula	$C_{26}H_{56}ClP$
Molecular weight	435.16
Structural formula	
Purity of the active ingredient	50 %

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Bellacide 350 Technical

Property	Result
Colour and physical state	white solid (as the solid) colourless liquid (as the (integrated system product) ISP)
Odour	practically odourless (as the ISP)
Melting range	not applicable to the ionic solid or ISP form of the active

Property	Result
Boiling point or range	not applicable to the ionic solid 104°C (as the ISP)
Density	1.06 g/mL (as the solid) 0.9542 g/mL (as the ISP)
Vapour pressure at 20°C	$< 5 \times 10^{-6}$ Pa at 39°C (for the solid)
Ultraviolet (UV)-visible spectrum	Very little absorption in the visible spectrum, absorption maxima at 275 nm ($\varepsilon \sim 5.35$ L/(mol cm))
Solubility in water at 20°C	> 1000 g/kg (for the solid)
Solubility in organic solvents at 20°C	Solvent — Solubility (g/kg) (for the solid) n-Heptane — 0.07 Acetone — > 250 Dichloromethane — > 250 Ethyl Acetate — > 250 Methanol — > 250 Toluene — > 250
n-Octanol-water partition coefficient (K_{ow})	Ionic species - partition coefficient will be negative
Dissociation constant (pK_a)	active will be present as the unassociated ions at environmental pH
Stability (temperature, metal)	ISP was stable on storage at 50°C for 30 days, product will not be stored in contact with metal

End-Use Product—Bellacide 350

Property	Result
Colour	clear colourless
Odour	slight sweet odour
Physical state	liquid
Formulation type	Solution
Guarantee	50%
Container material and description	HDPE drums or totes
Density	0.96 g/mL
pH of 1% dispersion in water	7.0–9.0
Oxidizing or reducing action	not expected to have appreciable oxidizing or reducing properties
Storage stability	no degradation in commercial containers on storage
Corrosion characteristics	no corrosion to commercial HDPE containers
Explodability	not expected to be explosive

1.3 Directions for Use

For the control of slime-forming and sulfate-reducing bacteria in injection waters during enhanced oil recovery and to reduce bacterial degradation of fracturing fluids used in oil and gas well stimulations, Bellacide 350 may be applied at 25–130 ppm.

1.4 Mode of Action

Tributyl tetradecyl phosphonium chloride disrupts microbial cell membranes, making them more permeable and causing important cell components to leak out, ultimately leading to death of the bacteria. This mode of action is consistent with all quaternary based biocides.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

A high-performance liquid chromatography method with tandem mass spectrometry (HPLC-MS/MS) was developed and proposed for data generation and enforcement purposes. This method fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The toxicology database for TTPC included acute toxicity and genotoxicity studies, a 90-day toxicity study in which rats were administered the test material in drinking water, and rat and rabbit gavage developmental toxicity studies. It was reported that drinking water was selected as the method of dose administration in the repeat-dose study due to binding of TTPC to fibrous components of the diet, resulting in insufficient extraction and recovery values. Waiver rationales were submitted in lieu of studies to address the chronic toxicity, carcinogenicity, and reproductive toxicity potential of TTPC, as well as to address the toxicokinetics of this chemical. All studies were conducted with test material containing 50% TTPC, with the exception of some acute toxicity studies that were conducted with test material containing 5% TTPC or with purified (approximately 94%) TTPC. For the purpose of this review, the administered dose levels in the repeat-dose studies were expressed in terms of the active ingredient content in the test material.

In acute toxicity testing, purified TTPC was of moderate toxicity via the oral route and of low toxicity via the dermal route in rats. It was corrosive to the eyes of rabbits. In rats, the 50% TTPC test material was moderately toxic via the oral route and of low toxicity via the dermal route. In acute inhalation toxicity testing, a 5% TTPC test material was slightly toxic to rats.

When considering the available information, it was possible to extrapolate the results of the latter study to a 50% TTPC solution. Based on this extrapolation, the 50% TTPC test material was considered highly toxic via inhalation. The 50% TTPC test material was corrosive to the eyes and skin of rabbits, and was negative for dermal sensitization in the guinea pig maximization test.

In the rat 90-day drinking water toxicity study, clinical signs included piloerection, rough fur, salivation, brownish discoloration of the muzzle and neck, hunched posture, penis prolapse, and vaginal discharge. Rats also exhibited an initial reduction in food consumption early in the study, as well as decreases in body weight, body weight gain, and water consumption throughout the study period. Alterations in several clinical chemistry parameters were evident in both sexes, and an increase in kidney weight was observed in females.

In the rat gavage developmental toxicity study, an increased incidence of incomplete ossification of sternebrae was observed in fetuses at a dose level that produced maternal toxicity, including decreased body weight gain and food consumption. Dyspnea was also observed in one dam. At the next higher dose level, an increased incidence of fusion of ribs, irregular ossification of sternebrae, and bipartite vertebral centres was observed. These findings occurred in the presence of severe (death) maternal toxicity. In the rabbit gavage developmental toxicity study, decreased fetal body weight and delayed ossification of the phalangeal nuclei of the forelimb and hind limb occurred at a dose level that was toxic to maternal animals, as demonstrated by body weight loss and decreased body weight gain and food consumption. An increase in the incidence of fused ribs and fused sternebrae was observed in fetuses at the next higher dose level. Additional findings in maternal animals at this dose level included isolated incidences of diarrhea.

Studies were conducted to evaluate the mutagenic and genotoxic potential of TTPC. No evidence of mutagenic potential was observed in an in vitro bacterial reverse mutation assay; however, this study was deemed supplemental since it did not include strains used to detect cross-linking agents, nor did it include adequate positive controls. TTPC was negative in in vitro assays for forward gene mutations in Chinese hamster V79 lung cells, and for DNA damage in rat hepatocytes and human fibroblasts. An in vivo micronucleus assay in Chinese hamsters was negative; however, limitations in reporting and study conduct were noted. Although negative results were obtained in the available genotoxicity studies, a more definitive determination of the genotoxic potential of TTPC is precluded by the limitations in some of the submitted assays as well as the lack of an assessment of clastogenic potential.

As noted above, study waiver rationales were provided by the applicant for toxicokinetic, reproductive toxicity, carcinogenicity, and chronic toxicity data. The submitted rationales for chronic toxicity, reproductive toxicity and carcinogenicity were based in part on the lack of significant exposure to TTPC from its proposed uses, and on the availability of toxicity data with analog chemicals. The rationale supporting the waiver for the requirement for toxicokinetic data was largely based on the argument that these data would not shed further light on the toxicity of TTPC.

The PMRA did not accept the applicant's waiver rationale regarding toxicokinetic data, since from a hazard characterization perspective, such information may be valuable in interpreting toxic effects, or lack thereof, and may assist in the extrapolation of animal toxicity data to humans. With regards to the other study waivers, the analog chemicals identified by the applicant were tetrakis (hydroxymethyl) phosphonium chloride (THPC) and tetrakis (hydroxymethyl) phosphonium sulfate (THPS), both of which have been tested for oncogenicity, genotoxicity, and short-term repeated oral toxicity under the National Toxicology Program in the United States. Additional toxicology information for THPC was summarized and reviewed by the National Research Council of the United States, and the International Agency for Research on Cancer evaluated the carcinogenic potential of THPS and THPC. The active ingredient THPS is registered for slimicide use in Canada, whereas THPC is not registered as a pesticide in Canada. Following an examination of the publicly available information on THPS and THPC, as well as the previous PMRA evaluation of THPS (Evaluation Report ERC2010-02, *Tetrakis (Hydroxymethyl) Phosphonium sulfate)*, the PMRA concluded that THPS and THPC are not adequate surrogates for the assessment of potential carcinogenicity, chronic toxicity, or reproductive toxicity of TTPC. This conclusion was based on dissimilarities in both structure and overall toxicological profiles between TTPC and the cited analogs, as well as limitations in the studies conducted with THPS and THPC. A more fulsome explanation of the PMRA's assessment of each of the submitted study rationales is included in relevant sections in Appendix I, Table 2.

Overall, it was not possible to fully characterize the potential human health effects of TTPC due to the limited toxicology database and unacceptability of the data waiver rationales. However, a qualitative approach to risk assessment was taken since exposure to TTPC in enhanced oil recovery systems and fracturing fluid systems was determined to be limited. For this reason, no additional toxicology studies were required for the current assessment. However, for future expansion of use of TTPC, the PMRA will reconsider the need for additional toxicology data.

Results of the toxicology studies conducted on laboratory animals with TTPC are summarized in Appendix I, Table 2. Toxicology reference values for use in human health risk assessment were not established since a qualitative approach to risk assessment was taken.

Incident Reports

Tributyl tetradecyl phosphonium chloride is a new active ingredient for use in Canada and as of 28 February 2018, no incident reports in humans or domestic animals have been reported to the PMRA. Once products containing TTPC are registered, registrants are required to submit any incidents that they receive.

3.1.1 Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, gavage rat and rabbit developmental toxicity studies were available. The waiver rationale submitted in lieu of a reproductive toxicity study was not accepted. Therefore, the database does not contain the standard required studies for assessing potential toxicity to infants and children.

With respect to potential prenatal and postnatal toxicity, there was no evidence of sensitivity of the young in the rat and rabbit developmental toxicity studies. In the rat study, incomplete ossification of sternebrae in fetuses occurred at a maternally toxic (including reduced body weights) dose level; serious effects (fused ribs) along with additional skeletal variations/delays in ossification occurred in fetuses at a higher dose level which resulted in maternal death. In the rabbit study, decreased body weight and delayed ossification of the limb phalanges occurred in fetuses at a dose level that was toxic (including body weight loss) to maternal animals. An increased incidence of a serious developmental effect (fused ribs, sternebrae) was observed at the next higher dose level.

Although no evidence of sensitivity of the young was observed in the rat and rabbit developmental toxicity studies, the database lacks a reproductive toxicity study. However, given the use pattern, the PCPA factor is not relevant since no dietary or residential exposure is anticipated. Although the PCPA factor is not relevant for the use pattern, it was important to give consideration to the fact that the worker population could include pregnant and nursing women. This was not a concern for the current assessment, however, since exposure was considered to be limited and a qualitative approach was taken for risk assessment.

3.2 Acute Reference Dose (ARfD)

The establishment of an ARfD is not required at this time as there are no proposed food uses, and contamination of drinking water is not expected.

3.3 Acceptable Daily Intake (ADI)

The establishment of an ADI is not required at this time as there are no proposed food uses, and contamination of drinking water is not expected.

Cancer Assessment

In the absence of oncogenicity studies, the potential for carcinogenicity of TTPC cannot be assessed. However, this assessment is not required at this time based on the proposed use pattern.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicology Reference Values and Endpoints

As the use of TTPC in enhanced oil recovery systems and fracturing fluid systems is expected to result in limited exposure, toxicology reference values were not required.

Occupational exposure to Bellacide 350 is characterized as intermediate-term for applicators and short-term for re-entry workers and is predominantly by the dermal and inhalation routes.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

There is potential for exposure to workers mixing/loading and applying Bellacide 350. Dermal and inhalation exposure estimates for workers handling Bellacide 350 in oilfield were qualitatively assessed.

Exposure to workers mixing, loading and applying Bellacide 350 is expected to be intermediate-term in duration and to occur primarily by the dermal and inhalation routes. The exposure estimates are based on mixers/loaders/applicators wearing coveralls worn over long-sleeved shirt and long pants, socks, chemical-resistant footwear, chemical resistant gloves, and protective eyewear (goggles or face mask).

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted.

Bellacide 350 has a low vapour pressure (5×10^{-9} kPa at 39°C; non-volatile) and is to be applied using closed metred delivery systems only. Open transfer systems are prohibited. Therefore, a mixer/loader/applicator quantitative risk assessment is not required as no risks of concern are expected, provided dry coupling is specified on the label.

3.4.2.2 Postapplication Worker Exposure and Risk

There is potential for exposure to workers re-entering areas treated with Bellacide 350. Bellacide 350 is used in oil and gas extraction operations to control microbial growth in enhanced oil recovery and fracturing fluids. Hydraulic fracturing is a technique in which rocks are fractured using pressurized liquid to help natural gas and petroleum flow more freely. Some (but not all) injected fluid is recovered through pipes and the flow back treated water is temporarily stored in open air pits or tanks. Eventually, the flow back water is transported to approved wastewater treatment and waste disposal facilities by trucks. Flow back water from fracturing operations is transported in sealed pressurized flow back equipment.

Typical activities for truck drivers transporting the flow back water includes hooking up hoses, filling their trucks, and hauling flow back water to an approved wastewater facility or underground injection site or deep well injection.

Tank entry and opening often requires a breathing apparatus. Depending on the size of the tank and operation, from four to thirty workers may be involved. When the tank is operational, there is no work ongoing or exposure. It is only when cleaning, re-coating, or bottom replacement when exposure could potentially occur. Depending on the activity, this can take hours to days.

Open air pits are also used to store flow back water to be reused or for later disposal. No specific work is usually performed around pits and tanks; however, oil field workers may be performing other activities in the vicinity of the pits. Given the nature of activities performed, it is unlikely that the workers would have any dermal contact with the open pits. Although potential inhalation exposure for postapplication re-entry workers may be possible from working around pits containing flow back water, limited exposure is expected due to the following:

- The fact that the pits are located outdoors where there is continual mixing with ambient air;
- Bellacide 350 has low vapour pressure at relatively high temperature (5×10^{-9} kPa at 39°C; non-volatile);
- Since Bellacide 350 biodegrades slowly in water (moderately persistent to persistent in water), the concentration of Bellacide 350 in the water is expected to decrease overtime to levels that would be much lower than those used during application; and
- Short-term and limited activities are expected to take place around pits.

Therefore, no inhalation risk of concern is expected for workers handling or working around pits containing Bellacide 350.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure to Bellacide 350 is not expected to be greater than the exposure to mixer/loader/applicator or postapplication workers.

Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current evaluation, the PMRA did not identify the potential for dietary or residential exposure for TTPC. Therefore, there is no requirement for a cumulative health risk assessment at this time.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

A summary of physical and chemical properties and environmental fate data for TTPC in the terrestrial and aquatic environments can be found in Appendix I, Tables 3–4.

Tributyl tetradecyl phosphonium chloride can enter the environment when used as a biocide for enhanced oil recovery systems and fracturing operations. Tributyl tetradecyl phosphonium chloride can also be mixed with other biocides to increase their effectiveness. Biocides used in fracking and enhanced oil recovery operations are exposed to unique environmental conditions

that are not relevant for other types of pesticide uses. Fracking fluid is a mixture of water and other chemicals (including biocides) that are injected 'downhole' after the drilling process is complete. It is possible for downhole temperatures to range from 150–300 degrees Celsius and downhole pressures to range from 703–2812 kg per square centimetre (10 000–40 000 pounds per square inch). Water that exists naturally in the rock formation tends to have a high salt content which can exceed that of seawater. It is expected that these extreme conditions (fracking/oil drilling) would cause degradation of chemical additives, such as biocides.

Produced water is the water or brine that exists naturally underground that accompanies the oil or gas that is extracted from underground wells. Flowback water refers to the fluids (fracking fluid plus produced water) returning to the surface of a well after hydraulic fracturing is complete. Once flowback water returns to the surface it is treated using processes that separate flowback water from a proppant (typically sand) and gas and oil. Flowback water is then either re-used or disposed of according to provincial regulations, which require disposal into an injection/disposal well. Flowback water is transferred from the drilling site to the disposal well either via tanker truck or through a produced water pipeline. Unintentional releases of flowback water to the environment may occur if there is a breach of the produced water pipeline. These releases occur over relatively small areas and are unlikely to occur at the same area more than once; as such, environment exposure is expected to be limited.

In the event of a release of produced/flowback water containing TTPC to the aquatic environment, TTPC would be expected to mix readily as it is very highly soluble (500 000 mg a.i./L) in water although it is not expected to remain in water, as the primary route of dissipation is expected to be sorption to sediment and organic matter. Once TTPC has adsorbed onto sediments, it will break down into two other chemicals, (tributyl-(5-hydroxy-pentyl) phosphonium chloride and tributyl-(7-hydroxy-heptyl) phosphonium chloride). Tributyl tetradecyl phosphonium chloride is considered to be moderately persistent to persistent in aerobic aquatic systems and non-persistent in aerobic water. Tributyl tetradecyl phosphonium chloride is considered stable to hydrolysis at environmentally relevant pH values and therefore, hydrolysis is not expected to be a significant route of transformation in waterbodies. In addition, TTPC is not expected to undergo photolysis. Based on its negligible vapour pressure, volatilization of TTPC from moist soil or water surfaces is not expected. As a result, long-range atmospheric transport is not expected as TTPC, and any potential environmental exposure is expected to be limited to the immediate area of release. Tributyl tetradecyl phosphonium chloride and its transformation products are expected be in equilibrium with organic and water phase (1:1) thus the resulting log K_{ow} would be zero. Based on this, TTPC and its transformation products are not expected to bioaccumulate.

In the event of a release of produced water containing TTPC to the terrestrial environment, the primary route of dissipation for TTPC is expected to be adsorption to soil particles. Tributyl tetradecyl phosphonium chloride has high soil adsorption coefficients (K_{oc} = 61 443–607 518), is highly adsorptive to soil and exhibits limited mobility. There were no data available to assess the rate at which TTPC may degrade in soil or what possible transformation products may result from degradation. It could be expected that biodegradation in soil may occur as it was observed to biodegrade in sediment.

Tributyl tetradecyl phosphonium chloride is classified as being immobile and is not expected to move into or leach into ground water. The method of Gustafson (1989) was also used to estimate the leaching potential of TTPC. The Groundwater Ubiquity Score values calculated for TTPC using these parameters was 1.3 which would classify TTPC as a non-leacher.

Monitoring data submitted by the registrant demonstrates a roughly 200-fold reduction in concentration of TTPC when measured in flowback water. It is not known if this mass loss can be attributed to thermal, pressure degradation, loss through microbial "consumption" (activity of the biocide) or through adsorption to particulate matter (sediment, other particulate material encountered in downhole conditions) or drill casing material (typically cement). Nonetheless these data indicate a substantial reduction in concentration of TTPC after use.

4.2 Environmental Risk Characterization

A summary of toxicity data for TTPC is presented in Appendix I, Table 5.

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models that take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e., protection at the community, population, or individual level).

Potential for Environmental Exposure

Tributyl tetradecyl phosphonium chloride was assessed by considering both the site of use (i.e., the physical site at which TTPC is added to fracking or enhanced oil recovery fluids) and post-use (i.e., during the flowback/produced water disposal process, assuming that flowback/produced water may contain TTPC).

Fracking or Enhanced Oil Recovery – Site of Use Scenario

At the drill site, TTPC may be added to fracking or oilfield flood (secondary recovery) fluids during different stages of the drilling/fracking process when needed to control microbial growth. For fracking processes, TTPC is added to the proppant along with water and other production chemicals in a mixing tank (slurry blender) prior to being pumped/injected downhole. At the site of use, lined ponds, storage tanks, or C-rings (above-ground walled storage systems) are the most common method of temporary storage of produced/flowback water.

A simple, conservative approach was used to determine EECs for the drilling site, assuming that if environmental exposure were to occur, it would be as a result of a tank/mixer breach spill. It was assumed that if such an event were to occur, the spill would be limited to the drilling site and that the concentration of TTPC would not be diluted i.e., that exposure to TTPC would occur at the maximum labelled application of 65 ppm (65 mg a.i./L).

Fracking or Enhanced Oil Recovery – Post-use Disposal Scenario

Tributyl tetradecyl phosphonium chloride can enter the environment after use as a biocide for fracking and enhanced oil recovery/water flooding operations during the disposal of produced/flowback water. After its use in fracking fluid, TTPC may return to the surface in produced/flowback water. Produced fluid/flowback water must be handled, stored, and disposed as per provincial regulations. This requires the transport of produced/flowback water to injection/disposal wells that are underground formations or depleted hydrocarbon pools. The method of transport for disposal of these fluids is either via tanker truck or through a produced water pipeline. There are two types of produced/flowback water pipelines i) temporary pipelines that can reach 5 km in length but typically 1–2 km in length and located near the tank farm where they store the materials and ii) permanent pipelines that carry produced water/flowback fluid that can go over hundreds of km. Due to the corrosive nature of produced water/flowback fluid, it has been documented that these pipelines fail and release fluid to the surrounding area. When failures occur, oil and gas operators are required to notify and report these incidents to relevant provincial authorities. Provincial data for produced water spill volumes were used to estimate environmental exposure for the post-use environmental exposure scenario.

Data derived from the Alberta Energy Regulator (AER) Incident Reporting website and other monitoring studies were used to refine the risk assessment (Appendix I, Table 8).

4.2.1 Risks to Terrestrial Organisms

A summary of terrestrial toxicity data for TTPC, is presented in Appendix I, Table 5. The screening and refined risk assessment for terrestrial organisms is presented in Appendix I, Tables 6–10.

For assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following exposure to TTPC. Toxicity information was available for acute and dietary toxicity to birds. No data were provided for soil dwelling organisms such as earthworms or terrestrial plants or terrestrial insects such as bees. These data are not required since it is expected that effects from the high salt content in potential produced water releases will eradicate plants and soil dwelling organisms such as earthworms or severely reduce their growth, if present, in the release area. Based on the Alberta Energy Regulator Incident Reporting website, the potential area affected for an inadvertent release of produced water is expected to be limited, reported releases are generally less than one hectare. It is assumed that these data are representative of potential releases in other provinces where this activity occurs.

Terrestrial vertebrates

Birds and mammals may be exposed to TTPC following the ingestion of plant materials and insects contaminated with TTPC after a release event. The terrestrial EECs calculated for TTPC residues were based on an assumption that exposure would occur from inadvertent releases to the terrestrial environment. The site of use risk assessment for TTPC was conducted assuming exposure may occur entirely through the consumption of food sources contaminated with TTPC at the maximum nomogram residue levels, the most conservative scenario. Concentrations of TTPC on different food guilds were calculated based on data collected from the Alberta Energy Regulators publicly available release incidents that occurred from the time data collection began (2013) to the time of assessment (early 2018). All data relevant to produced water were compiled and from the volume of releases an 80th percentile value (m^3) was calculated and used as the basis for estimating environmental exposure. For the initial screening level estimates of exposure a conservative assumption was made regarding the concentration of dosed TTPC such that TTPC does not undergo degradation during its downhole residence time and would return to the surface at the same concentration without degradation. The resulting conservative, screening level terrestrial EEC was 1950 g a.i./ha.

Birds

Tributyl tetradecyl phosphonium chloride can be classified as slightly toxic on an acute and dietary basis to Bobwhite Quail (surrogate species for terrestrial birds) and as highly toxic on an acute basis to Mallard duck (surrogate for aquatic birds). All bird toxicity studies were conducted with TTPC technical grade active ingredient. No reproduction studies were required as chronic exposure to TTPC residues is not expected. The risk quotients (RQs<1) for acute exposure to birds at the screening level risk assessment exceeded the LOC (level of concern) for various sized birds of certain feeding guilds (Appendix I, Table 9). A refined risk assessment was conducted which considered more realistic exposures based on data from provincial incident reports for produced water releases, monitoring data and mean nomogram residues. This refined assessment indicated no risk to birds. Therefore, the use of TTPC in fracking fluid and enhanced oil recovery/water flooding is not expected to pose a risk to birds.

Mammals

The laboratory toxicity of TTPC to rats was used to assess risk to small wild mammals. The results of the acute toxicity test suggest that TTPC is slightly toxic to rats (Appendix I, Table 2). In the rat reproduction study, the maternal NOAEL and developmental NOAEL endpoints were identical (10 mg TTPC/kg bw/day). The risk assessment for mammals was conducted using these two endpoints (acute LD_{50}: 501 mg a.i./kg bw/day and NOAEL for reproduction: 10 mg a.i./kg bw/day) and are presented in Appendix I, Table 7 and Table 9, respectively.

The screening RQs for acute exposure to mammals (all sizes) and on a reproductive basis exceeded the LOCs for various sized mammals of certain feeding guilds. Therefore, a refined risk assessment was conducted which considered more realistic exposures based on monitoring information from provincial incident reports for produced water releases, monitoring data and mean nomogram residues. This refined assessment indicated no risk to mammals. Therefore, the use of TTPC in fracking fluid and enhanced oil recovery/water flooding is not expected to pose a risk to small, wild mammals.

4.2.2 Risks to Aquatic Organisms

A summary of aquatic toxicity data for TTP is presented in Appendix I, Table 5.

For assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following exposure to TTPC. Toxicity information was available for freshwater; fish, invertebrates, algae, and marine fish. The available studies show that TTPC is very highly toxic to fresh, warm water fish, highly toxic to fresh, cold water and marine fish and moderately toxic to marine invertebrates. No data were available for marine algae but data were not required for the proposed use pattern.

Site of Use Scenario – Screening Level Assessment

A conservative risk assessment was conducted assuming that 100% of TTPC added to fracking fluids would still be present in the process fluids returned to the surface after drilling or enhanced oil recovery/water flooding operations and that these fluids would be deposited directly to water surfaces at the site of use. The resulting LOC was exceeded for all aquatic organisms (freshwater aquatic invertebrates, fresh, cold-water fish, fresh water algae, marine fish and amphibians) with the exception of marine invertebrates.

The aquatic EECs calculated for TTPC residues were based on an assumption that exposure would occur from inadvertent releases of produced water to surface water and ephemeral wetlands, that these habitats would be present at the site of use and that the amount of TTPC dosed in fracking fluid would remain unchanged after downhole residence time. The estimate of exposure was derived from provincial incident data. For surface waters, direct release was assumed for a water body of 1 ha in area and a depth of 80 cm for spills to aquatic habitat for all aquatic organisms except for amphibians, where a water depth of 15 cm was assumed. In both scenarios, complete mixing and dilution by the water body was assumed.

The level of risk to aquatic organisms was estimated using surface water EECs. There were exceedances of the LOC for all freshwater organisms (invertebrates, cold and warm freshwater fish, freshwater algae, freshwater vascular plants or marine fish) with the exception of marine invertebrates.

Although this assessment indicated a potential for risk to non-target organisms at the site of use during fracking or oil recovery operations, additional mitigation measures are not required for the following two reasons.

i) These use sites are industrial operations and not considered habitat for non-target organisms.

ii) Drilling/fracking sites are constructed with extensive engineering controls in place that are intended to protect the environment surrounding the use site. These measures are required by provincial regulations and include the use of physical berms to contain accidental spills of liquids including production chemicals such as TTPC. In the event of a spill on site, there are provincial regulations governing clean up, site reclamation with follow up monitoring and compliance by relevant provincial authorities. For an excerpt of such requirements please refer to the Alberta Energy Regulator Directive 050 (2016). Other provinces have similar requirements and in some cases refer to Alberta Energy Regulator Directive 050.

Post-use disposal pipeline – screening level assessment

Potential for environmental exposure exists during disposal activities when produced/flowback water is carried to disposal wells in produced water pipelines. An initial, conservative risk assessment was conducted that assumed TTPC would not break down during use in fracking or enhanced oil recovery operations and would return the surface and hence flowback/produced water in the same concentration as the initial dose of 65 ppm. The volume of release considered was the 80th percentile calculated from the provincial incident reports. The resulting risk quotients exceeded the LOC, indicating potential acute risk to aquatic organisms (RQs ranged from 0.31 for aquatic algae to 224 for amphibians).

Post-use disposal– refined assessment

A refined risk assessment was conducted that considered more relevant exposure concentrations of TTPC. These were obtained by using monitoring information from provincial incident reports for produced water releases and monitoring data. This refined assessment indicated no acute risk to aquatic organisms with risk quotients ranging from 0.007 (freshwater aquatic invertebrates) to 0.17 (amphibians). Therefore, the use of TTPC in fracking fluid and enhanced oil recovery/water flooding is not expected to pose a risk to aquatic organisms.

4.2.3 Incident Reports

Tributyl tetradecyl phosphonium chloride is a new active ingredient for use in Canada and, as of 24 January 2018, there are no environment incident reports. Once products containing tributyl tetradecyl phosphonium chloride are registered, registrants are required under the Pest Control Products Incident Reporting Regulations to submit any incidents that they receive.

5.0 Value

Uncontrolled microbial growth in oilfield operations can result in significant economic losses due to process inefficiencies caused by biofilms, oilfield "souring" and microbially induced corrosion of equipment. Slimicides are used in oilfield settings to reduce the frequency and severity of biofilm forming within process fluids and the problems that it causes.

There are several slimicides based on 15 different active ingredients currently registered in Canada for use in oilfield water injection systems and fracturing fluids. These slimicides represent a range of chemistries and modes of action from oxidizing biocides to quaternary ammonium compounds that act on cell membranes to glutaraldehyde that reacts with proteins.

Having alternative slimicides with differing modes of action is important in ensuring that effective products are available that can address the variety of oilfield sites with differing geology and microbial flora. Alternating slimicides with different modes of action is also useful in preventing microbial resistance from forming. Bellacide 350 provides another slimicide option based on a new chemistry and is compatible with current management practices.

Data were provided from laboratory trials that demonstrated the performance of Bellacide 350 against common oilfield bacteria, such as sulphate reducing bacteria (SRB) and acid producing bacteria (APB). In one study, samples of fracturing fluid were treated with Bellacide 350 and surviving bacteria were counted following treatment at time intervals ranging from 30 minutes to seven days. When applied at a rate of 30 ppm active ingredient, Bellacide 350 reduced microbial levels of planktonic bacteria by > 99.9% after 24 hours.

In another study, Bellacide 350 treatment at 50 ppm of active ingredient was required to effectively remove biofilm after four hours. Its effectiveness was comparable to biofilm removal properties exhibited by other active ingredients which are registered for use in oilfield applications.

Use history case studies were provided for an oilfield in Nebraska and elsewhere in North America. The Nebraska site was experiencing significant microbial fouling issues resulting in a decreased output, and significant economic losses. The biocide program they had been using, based on a quaternary ammonium biocide, was replaced by treatment with Bellacide 350 for a 3 month period. At a treatment rate of 30 ppm active ingredient, Bellacide 350 was able to control and maintain microbial growth in the well at an acceptable level.

Bellacide 350 is incompatible with polyvinyl chloride (PVC) plastics. No other non-safety adverse effects from the use of Bellacide 350 have been reported or identified.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, those that meet all four criteria outlined in the policy, i.e., persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.

During the review process, TTPC was assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Tributyl tetradecyl phosphonium chloride does not meet Track 1 criteria, although insufficient information is available to determine if it forms any transformation products which meet the Track 1 criteria. See Appendix I, Table 13 for comparison with Track 1 criteria. Available fate data indicates that TTPC will not partition to air and it does not meet the bioaccumulation criteria.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[8] and takes into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under the New *Pest Control Products Act.*

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

- Technical grade tributyl tetradecyl phosphonium chloride and its end-use product Bellacide 350 do not contain any contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

Overall, the toxicology database for TTPC is limited, lacking studies for the assessment of toxicokinetics, chronic toxicity, carcinogenicity, and reproductive toxicity. In the available studies, there was no evidence to suggest that TTPC was genotoxic; however, limitations were noted in the available genotoxicity battery. There was no evidence of increased susceptibility of the young in the developmental toxicity studies. The primary effects observed in adult animals given oral doses of TTPC included decreased body weight and clinical signs of toxicity. However, given that exposure to TTPC was determined to be limited based on the use in enhanced oil recovery systems and fracturing fluid systems, no further toxicology studies were required to complete the current assessment.

Mixer, loader applicators handling Bellacide 350 and workers re-entering treated areas in oilfield are expected to be exposed to levels of Bellacide 350 that will result in an acceptable risk when the Bellacide 350 is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

Occupational exposure to Bellacide 350 when used according to label directions is not likely to result in any human health concern.

7.2 Environmental Risk

The use of TTPC as a biocide according to the label directions does not pose risks of concern to the environment.

Standard precautionary label statements to inform users of the toxicity to aquatic organisms will be added to the label. In addition, a label statement to mitigate risk will be required stating that effluent containing this active ingredient, from use of TTPC in fracking fluid and enhanced oil recovery/water flooding, should not be discharged into waterbodies.

7.3 Value

Biocides are important to protect process fluids in a number of oilfield operations, particularly fracturing fluids and water flooding used for enhanced oil recovery. Due to the wide diversity in geological and microbial makeup of oilfield sites, it is important to have a number of different biocides with different modes of action to ensure there are viable treatment options and to help prevent the formation of antimicrobial resistance. Bellacide 350 provides a new chemistry to the biocides registered for oilfield uses.

8.0 Proposed Regulatory Decision

Under the authority of the *Pest Control Products Act* and Regulations, the PMRA is proposing registration for the sale and use of Bellacide 350 Technical and Bellacide 350, containing the technical grade active ingredient tributyl tetradecyl phosphonium chloride, to control microbial slime formation in enhanced oil recovery systems and fracturing fluid systems.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products is acceptable.

List of Abbreviations/Glossary

↑	increase
↓	decrease
♂	male
♀	female
µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
AER	Alberta Energy Regulator
a/g	albumin/globulin
ALS	acetolactate synthase
APB	acid producing bacteria
AR	applied radioactivity
ARfD	acute reference dose
atm	atmosphere
BUN	blood urea nitrogen
bw	body weight
bwg	bodyweight gain
C	Celsius
C-rings	above-ground walled storage systems for the temporary storage of saline fluids that result from or for use in hydraulic fracturing
CAS	Chemical Abstracts Service
C.I.	confidence interval
cm	centimetres
d	day(s)
DACO	data code
DAT	days after treatment
DF	dry flowable
DFO	double first-order
DIR	Regulatory Directive
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
EC_{50}	effective concentration on 50% of the population
EEC	Estimated environmental concentration
ER	Evaluation Report
Fracturing fluid	A fluid injected underground into a well to extract hydrocarbons.
Flowback water	A collective term that refers to the fluids returning to the surface of a well after hydraulic fracturing is complete; includes produced water.
FC	food consumption
g	gram
GD	gestation day
h	hour

ha	hectare(s)
HDPE	high density polyethylene
HDT	highest dose tested
Hg	mercury
HPLC-MS/MS	high performance liquid chromatography method with tandem mass spectrometry
Hydraulic fracturing	A technology used to stimulate hydrocarbon reservoirs that pumps liquids at high pressure down a well to fracture and shatter the formation rock.
IA	Iowa
IORE	indeterminate-order rate equation
ISP	integrated system product
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
kPa	kiloPascal
L	litre(s)
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEC	lowest-observed-adverse-affect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	low observed effect concentration
LOQ	limit of quantitation
mg	milligram(s)
mL	millilitre
MAS	maximum average score
MIS	maximum irritation score
MOE	margin of exposure
mol	mole
MRL	maximum residue limit
MS	mass spectrometry
n/a	not applicable
ND	North Dakota
ng	nanogram
nm	nanometre
NOAEC	no-observed-adverse-effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
OC	organic carbon content
OM	organic matter content

Pa	Pascal
PBI	plantback interval
PCPA	*Pest Control Product Act*
pH	measure of the acidity or basicity of an aqueous solution
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
Primary oil recovery	water or brine that exists naturally underground that accompanies the oil or gas that is extracted from underground wells.
PVC	polyvinyl chloride
RQ	risk quotient
RSD	relative standard deviation
SC	soluble concentrate
SFO	single first-order
SRB	sulfate reducing bacteria
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
Tertiary recovery	Oil production is separated into three phases: primary, secondary and tertiary, which is also known as Enhanced Oil Recovery (EOR). Tertiary recovery also known as enhanced oil recovery uses thermal recovery, gas
TGAI	technical grade active ingredient
THPC	tetrakis (hydroxymethyl) phosphonium chloride
THPS	tetrakis (hydroxymethyl) phosphonium sulfate
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
TTPC	tributyl tetradecyl phosphonium chloride
TX	Texas
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environnemental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
WA	Washington state
wt	weight

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Sediment	035197-1	parent	HPLC-MS/MS	2 ng/g (ppb)	2733378

Table 2 Toxicity Profile of Tributyl Tetradecyl Phosphonium Chloride (TTPC)

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted.)

Study Type/ Animal/PMRA #	Study Results
Toxicokinetics Waiver request PMRA #2447865	**Applicant's Waiver Rationale:** The waiver was based on the lack of significant exposure, the lack of unusual effects or an unusually steep dose-response for TTPC toxicity, and the ability to well define and control TTPC-associated risks on the basis of existing data. **PMRA Conclusions:** The assertion that the generation of toxicokinetic data will not shed further light on the toxicity of TTPC is not accepted from a hazard characterization perspective given the valuable information obtained from toxicokinetics studies. However, data are not required at this time since exposure to TTPC in enhanced oil recovery and fracturing fluid systems was determined to be limited.
Acute oral Rat (Tif:RAIf) PMRA #2447851	Tested with ~94% TTPC Supplemental LD_{50} = 611 mg/kg bw Clinical signs included sedation, dyspnea, exophthalmos, ruffled fur, diarrhea, and curved body position. **Moderate Toxicity**
Acute oral Rat (Tif:RAIf) PMRA #2447850	Tested with 50% TTPC LD_{50} (♂) = 1279 mg/kg bw LD_{50} (♀) = 802 mg/kg bw LD_{50} (♂/♀) = 1002 mg/kg bw Clinical signs included dyspnea, exophthalmos, ruffled fur, curved body position, sedation, and diarrhea. **Moderate Toxicity**

Study Type/ Animal/PMRA #	Study Results
Acute dermal Rat (Tif:RAIf) PMRA #2447856	Tested with ~94% TTPC Supplemental LD_{50} (♂) > 4000 mg/kg bw LD_{50} (♀) > 3000 and < 4000 mg/kg bw LD_{50} (♂/♀) ≈ 4000 mg/kg bw Clinical signs included sedation, dyspnea, ruffled fur, and curved body position. Edema and necrosis were observed at the application site. **Low Toxicity**
Acute dermal Rat (Tif:RAIf) PMRA #2447852	Tested with 50% TTPC LD_{50} > 2000 mg/kg bw Clinical signs included sedation, dyspnea, exophthalmos, ruffled fur, and curved/ventral body position. Severe necrosis occurred at the application site, increasing in severity over time until the entire treated area of skin was dead. At 14 days, the dead skin started to slough off, exposing the underlying muscular layer. **Low Toxicity**
Acute inhalation Rat (Sprague Dawley) PMRA #2447857, #2447858	Tested with 5% TTPC LC_{50} (♂) = 1.0 mg/L LC_{50} (♀) = 0.8 mg/L LC_{50} (♂/♀) = 0.9 mg/L Clinical signs included rales, laboured breathing, red material around the nose/mouth, clear material around the mouse/nose/eyes, gasping, unkempt appearance, locking/lurching/swaying while walking, hypoactivity, hypothermia, decreased defecation. **Slight Toxicity** Tested with 50% TTPC Extrapolated LC_{50} = 0.088 mg/L All rats exposed to 3.3 mg/L died within 90 minutes of the initiation of exposure. Both rats exposed to 1.12 mg/L died within 120 minutes of the initiation of the exposure period, and both rats exposed to 0.20 mg/L were found dead on the day following exposure. No clinical observations were conducted during the exposure period. **Considered of High Toxicity**

Study Type/ Animal/PMRA #	Study Results
Eye irritation Rabbit (New Zealand White) PMRA #2447860	Tested with ~94% TTPC Supplemental Unwashed eyes: MAS (24, 48, 72 hours) = 108 MIS = 110 at 24 and 48 hours Washed eyes: MAS (24, 48, 72 hours) = 103 MIS = 110 at 24 and 48 hours Rinsing eye had little effect on irritation reaction. Study was terminated after 7 days. **Corrosive to eyes**
Eye irritation Rabbit (New Zealand White) PMRA #2447859	Tested with 50% TTPC Unwashed eyes: MAS (24, 48, 72 hours) = 99 MIS = 103 at 48 hours Washed eyes: MAS (24, 48, 72 hours) = 92 MIS = 96 at 72 hours Rinsing the eye had little effect on irritation reaction. Study was terminated after 72 hours. **Corrosive to eyes**
Skin irritation Rabbit (New Zealand White) PMRA #2447863	Tested with 50% TTPC Supplemental Intact skin MAS (24, 48, 72 hours) = 7.6 MIS = 7.7 at 48 and 72 hours Abraded skin MAS (24, 48, 72 hours) = 7.7 MIS = 7.8 at 48 and 72 hours Study terminated after 72 hours due to severe skin irritation. **Corrosive to skin**

Study Type/ Animal/PMRA #	Study Results
Dermal sensitization (Maximization) Guinea pig (Dunkin Hartley) PMRA #2447864	Tested with 50% TTPC **Negative**
90-day oral toxicity (drinking water) Rat (Tif:RAIf) PMRA #2468942, #2836319	Tested with 50% TTPC NOAEL = 8.7/11 mg TTPC/kg bw/day LOAEL = 27/32 mg TTPC/kg bw/day Effects at the LOAEL: clinical signs (piloerection, rough fur, salivation, brownish discoloration on muzzle and neck, hunched posture, penis prolapse, vaginal discharge), ↓ bw, ↓ bwg, ↓ fc weeks 1–2, ↓ water consumption, ↑ BUN, ↓ cholesterol, ↓ calcium, ↑ chloride, ↑ globulin, ↓a/g ratio (♂/♀); ↓ albumin, ↓ prothrombin time, ↑ kidney wt (♀).
Chronic toxicity/ oncogenicity Waiver request PMRA #2447865	**Applicant's Waiver Rationale:** The waiver for chronic toxicity and oncogenicity studies was based on the lack of significant exposure associated with the proposed uses of TTPC, the lack of structural and biological characteristics associated with oncogenic potential, and adequate chronic toxicity and oncogenicity studies conducted with analog chemicals. **PMRA Conclusions:** The applicant's waiver rationale focused on the carcinogenic potential and lacked information related to the non-cancer chronic toxicity hazard assessment. The analog chemicals were not considered to be appropriate analogs for read-across extrapolation. No positive results were obtained in the battery of genotoxicity studies provided for TTPC; however, several limitations in these studies were noted. Information is limited to assess other biological characteristics associated with oncogenic potential. Therefore, the waiver rationale is not accepted from a hazard characterization perspective. However, data are not required at this time since exposure to TTPC in enhanced oil recovery and fracturing fluid systems was determined to be limited.
Reproductive toxicity Waiver request PMRA #2447865	**Applicant's Waiver Rationale:** The waiver for a reproductive toxicity study was based on the lack of significant exposure associated with the proposed uses of TTPC, the lack of reproductive toxicity in studies with structural analogs, and the lack of reproductive effects in available studies with TTPC. **PMRA Conclusions:** A reproduction study assesses unique endpoints that are not evaluated in other studies. The identification of target organs for TTPC is hindered by the paucity of toxicity studies, including toxicokinetic data. Several reproductive tissues were not assessed in the available 90-day oral toxicity study in rats (epididymides, prostate, seminal vesicles, uterus, vagina, pituitary gland). The analog chemicals were not considered to be appropriate analogs for read-across extrapolation. Therefore, the waiver rationale is not accepted from a hazard characterization perspective. However, data are not required at this time since exposure to TTPC in enhanced oil recovery and fracturing fluid systems was determined to be limited.

Study Type/ Animal/PMRA #	Study Results
Developmental toxicity (gavage) Rat (Sprague Dawley) PMRA #2468934, #2468938, #2468939, #2836320	Tested with 50% TTPC **Maternal Toxicity** NOAEL = 10 mg TTPC/kg bw/day LOAEL = 30 mg TTPC/kg bw/day Effects at the LOAEL: ↓ bwg GD 6–15, ↓ fc GD 6–11, dyspnea GD 15 in 1 ♀. Effects at the next highest dose level of 60 mg TTPC/kg bw/day: 2 deaths (GD 9 and 14), ↓ bw GD 9 and 15, dyspnea GD 15 in 4 ♀. **Developmental Toxicity** NOAEL = 10 mg TTPC/kg bw/day LOAEL = 30 mg TTPC/kg bw/day Effects at the LOAEL: ↑ fetal and litter incidence of incomplete ossification of the 5th sternebra. Effects at the next highest dose level of 60 mg TTPC/kg bw/day: ↑ fetal and litter incidence of skeletal findings: malformations (fusion of ribs; 2 fetuses in 2 litters versus none in the other groups, including controls), irregular ossification of sternebrae, bipartite vertebral centres. Developmental toxicity in the presence of maternal toxicity
Developmental toxicity (gavage) Rabbit (Chinchilla) PMRA #2447868, #2447871, #2468940, #2836320	Tested with 50% TTPC **Maternal Toxicity** NOAEL = 3.8 mg TTPC/kg bw/day LOAEL = 11 mg TTPC/kg bw/day Effects at the LOAEL: bw loss GD 6–9, ↓ bwg GD 6–18, ↓ fc GD 6–15. Effects at the next highest dose level of 23 mg TTPC/kg bw/day: diarrhea in 2 ♀ GD 8 or 17. **Developmental Toxicity** NOAEL = 3.8 mg TTPC/kg bw/day LOAEL = 11 mg TTPC/kg bw/day Effects at the LOAEL: ↓ fetal bw (5–11%), delay in ossification of the phalangeal nuclei of the forelimb (↑ fetal and litter incidence of absent ossification) and hindlimb (↑ fetal incidence of absent ossification). Effects at the next highest dose level of 23 mg TTPC/kg bw/day: slight ↑ fetal and litter incidence of irregular ossification of sternebrae and skeletal malformations (fusion of ribs/sternebrae; 3 fetuses in 3 litters versus none in the other groups, including controls). Developmental toxicity in the presence of maternal toxicity

Study Type/ Animal/PMRA #	Study Results
Bacterial reverse mutation *S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538 PMRA 2447872	Tested with 50% TTPC Supplemental (inadequate positive controls; strain for detecting cross-linking agents not used) No evidence of induced mutant colonies over background under the tested conditions Tested up to cytotoxic concentrations.
In vitro forward mutation in mammalian cells Chinese hamster V79 lung cells PMRA #2447873	Tested with 50% TTPC **Negative** Tested up to cytotoxic concentrations.
In vivo micronucleus assay Chinese hamster PMRA #2447874	Tested with 50% TTPC Supplemental (limitations in study reporting and conduct) No evidence of induced micronuclei over background under the tested conditions 76 mg/kg bw/day: 1 ♀ died.
DNA repair Rat hepatocytes PMRA #2468944	Tested with 50% TTPC **Negative** Tested up to cytotoxic concentrations.
DNA repair Human fibroblasts PMRA #2468945	Tested with 50% TTPC **Negative** Tested up to cytotoxic concentrations.

Table 3 Fate and Behaviour in the Environment

PMRA Study Number #	Study Title	Rating	Study Endpoints
#2447877	Hydrolysis of Belclene 350	Supplemental	hydrolytically stable at pH values of 5, 7, and 9 at 25°C (30 days).
#2447878	Photodegradation of Belclene 350 in Water	Reliable with restrictions	Stable (15 days continuous light exposure)

PMRA Study Number #	Study Title	Rating	Study Endpoints
#2646615/#2733381	Aerobic Aquatic Metabolism of [14C]Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC)	Reliable with Restrictions	Goose River (EFS-485) Half-life = 299 days (SFO; 20°C); DT_{50} = 299 days; DT_{90} = 993 days (SFO) Bonne Femme Creek (EFS-486) Half-life = 50.6 days (20°C; DFOP); DT_{50} = 73.4 days; DT_{90} = 819 days (DFOP)
#2733380	Aerobic Aquatic Metabolism of [^{14}C]Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC)	Fully Reliable	Goose River (EFS-485) Half-life = 371 days (IORE); DT_{50} = 7.83 days; DT_{90} = 1232 (IORE) Bonne Femme Creek (EFS-486) Half-life = 191 (IORE); DT_{50} = 11.9 days; DT_{90} = 634 days (IORE)
#2447880	The Test for Biodegradability of TK12 780/0 OECD Closed Bottle Test No. 301D	Reliable with restrictions but does not satisfy the requirement for acrobic biodegradation in water or soil	Tributyl tetradecyl phosphonium chloride not readily biodegradable by a mix of bacteria found in secondary sewage effluent and soil
#2447881	Adsorption/Desorption	Unreliable	Major study deficiencies were noted that prevent use of the results, including no soil characterization (sand/silt/clay content; pH values (in 0.01 M CaCl); organic carbon content; Cation Exchange Capacity (mmol/kg)
#2646618	Adsorption/Desorption Properties of [14C] Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC) in Six Soils	Reliable	EFS-416 Clay loam Grand Forks County, ND (3.4% OC; pH 5.2; CEC: 19.5; 35% sand; 33% silt; 32% clay) Kd Koc Kf KF OC 1/n 2837 83432 2082 61249 0.9488 EFS-460 Maverick County, TX Silty clay loam (1.9% OC; pH 7.7; CEC: 17.2; 36% sand; 49% silt; 15% clay) Kd Koc Kf KF OC 1/n 1254 67536 1619 87202 1.0468 EFS-469 Grand Forks County, ND Sandy

PMRA Study Number #	Study Title	Rating	Study Endpoints
			loam (2.3 % OC; pH 6.8; CEC: 17.3; 63% sand; 19% silt; 18% clay) Kd Koc Kf KF OC 1/n 1742 77011 1693 74852 0.9970 EFS-470 Killsbury, IA Silt loam (2.1% OC; pH 7.3; CEC: 14.2; 17% sand; 61% silt; 22% clay) Kd Koc Kf KF OC 1/n 1319 61443 1588 73995 1.0326 EFS-476 Grand Forks County, ND Loamy sand (0.81% OC; pH 5.3; CEC:9.9; 81% sand; 9% silt; 10% clay) Kd Koc Kf KF OC 1/n 3078 379981 2947 363830 0.9933 EFS-442 Ephrata, WA Loamy sand (0.23% OC; pH 7.0; CEC:13.2; 77% sand; 19% silt; 4% clay) Kd Koc Kf KF OC 1/n 1397 607518 2774 1205878 1.1213

Table 4 Summary of major transformation products (>10% applied radioactivity) formed in the submitted environmental studies

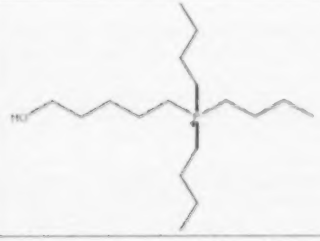
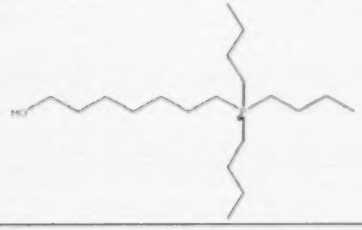
Structure	Major Transformation Product name (Nomenclature)	Study Type	Max % of Applied, days after treatment (DAT)	PMRA Number(s)
	Tributyl-(5-hydroxy-pentyl)-phosphonium C17H38OP+ 289.27 (exact mass)	Aerobic aquatic	*Reported collectively as Metabolite A* > 10% AR, 30 DAT	#2646615
	Tributyl-(7-hydroxy-heptyl)-phosphonium C19H42OP+ 317.30	Aerobic aquatic	*Reported collectively as Metabolite A* > 10% AR, 30 DAT	#2646615

Table 5 Toxicity of Tributyl Tetradecyl Phosphonium Chloride to Non-Target Species – Aquatic and Terrestrial

PMRA Number #	Study Title	Study Endpoints
#2447884	Report on the test for Acute Toxicity of TK 12780/2 to *Daphnia magna*	24-h EC_{50} = 0.054 mg a.i/L; NOEC = 0.029 mg a.i/L; based on immobilization
#2651092	A Flow Through Life-Cycle Toxicity Test with the Cladoceran (*Daphnia magna*)	NOEC: 0.0079 mg a.i./L Endpoints affects: growth in terms of total length, mean number of neonates produced per adult, immobility
#2447885	Belclene 350: Determination of the Acute Toxicity to Brown Shrimp (*Crangon crangon*).	Test: Static renewal 96-h LC_{50} = 1.59 mg a.i./L, 95% C.I. = 1.22–2.02 NOEC not observed (mortalities at lowest test concentration) Endpoints effected: mortality
#2447887	Test for Acute Toxicity of TK 12780/2 to Rainbow trout (*Salmo gairdneri*)	96-h LC_{50}: 0.40 mg a.i/L 95% C.I.: 0.36–0.45 mg a.i /L 96-h NOEC:0.050 mg a.i /L Probit Slope: n/a LOEC: 0.090mg a.i /L Endpoint(s) Effected: sub-lethal effects abnormal swimming behaviour and loss of pigmentation
#2447889	Test for Acute Toxicity of TK 12780/2 to Bluegill	96-h LC_{50}: = 0.058 mg a.i/L 95% C.I.: 0.044–0.074 mg a.i./L 96-h NOEC: 0.032 mg a.i /L Probit Slope: n/a Endpoint(s) Effected: sublethal endpoint was based on abnormal swimming behaviour
#2447894	Acute Oral LD_{50} – Mallard Duck D17-516	LD_{50}: 232 mg a.i./kg bw 95% C.I.: 118–322 mg a.i./kg bw Classified as Highly toxic on an acute basis. NOAEL: could not be established, effects were reported at all dosage levels. Endpoints affected: Mortality, lethargy, reduced reaction to external stimuli, loss of coordination, lower limb weakness, wing droop, prostrate posture, loss of righting reflex and depression.
#2447895	Eight Day Dietary LC_{50} – Bobwhite Quail D17-516	LC_{50}: 4215 mg a.i./kg diet (1663 mg a.i./kg bw/day) 95% C.I.: 3430–5184 mg a.i./kg diet (1324–2080 mg a.i./kg bw/day) Classified as Slightly toxic on a dietary basis.

PMRA Number #	Study Title	Study Endpoints
		NOAEC: not observed, treatment related effects at all test levels LOAEC: not observed, treatment related effects at all test levels Endpoints affected: Mortality, lethargy, reduced reaction to external stimuli, ruffled appearance, wing droop and lower limb weakness
#2447896	Eight Day Dietary LC_{50} – Mallard Duck	LC_{50}: 3663 mg a.i./kg diet (155 mg a.i./kg bw/day) 95% C.I.: 2749–5204 mg a.i./kg diet (116–220 mg a.i./kg bw/day) Classified as slightly toxic on a dietary basis NOAEC: not observed, treatment related effects at all test levels LOAEC: not observed, treatment related effects at all test levels Endpoints affected: Mortality, lethargy, reduced reaction to external stimuli, wing droop and lower limb weakness
#2447897	Determination of the effect of Bellacide 350 on the growth of fresh water green alga *Selenastrum capricormutum*	Test Type: 72-h; Static NOEC: 1.05 ug a.i./L (0.001 mg a.i./L) 72-h E_rC_{10}/ IC_{10}: 2.3 ug a.i./L (0.002 mg a.i./L; 95% C.I. not reported) 72-h E_rC_{50}/ IC_{50}: 8.7 ug a.i./L (0.009 mg a.i./L; 95% C.I. = 7.1–11 ug a.i./L) Endpoint Effected: growth rate 72-h E_bC_{10}/ IC_{10}: 0.49 ug a.i./L (0.005 mg a.i./L; 95% C.I. = 0.24–1.0 ug a.i./L) 72-h E_bC_{50}/ IC_{50}: 2.4 ug a.i./L (0.002 mg a.i./L; 95% C.I. = 1.0–3.2 ug a.i./L) Endpoint Effected: area under the growth curves
#2733376	A 7-Day Static Test Renewal Toxicity Test with Duckweed (*Lemna gibba G3*) – Final Report.	Test Type: 7-dat; Static renewal NOEC: 5.2 ug a.i./L 7-day E_bC_{10}: 12 ug a.i./L (95% C.I. = 7.3-21 ug a.i./L) 7-day E_bC_{50}: 59 ug a.i./L (95% C.I. = 47-73 ug a.i./L) Endpoint Effected: biomass yield 7-day EC_{10}: 13 ug a.i./L (95% C.I. = 7.2-22 ug a.i./L) 7-day EC_{50}: 57 ug a.i./L (95% C.I. = 45-73 ug a.i./L) Endpoint Effected: frond yield

Table 6 Screening level risk assessment for Tributyl Tetradecyl Phosphonium Chloride on non-target aquatic species

Risk quotients PMRA #	Species	Type of test	Toxicity endpoint adjusted for uncertainty (mg a.i./L)	EECs (mg a.i./L)		Risk Quotients
				15 cm depth	80 cm depth	
#2447884	*Daphnia magna*	Acute	0.027	n/a	0.24	9.04*
#2651092	*Daphnia magna*	Chronic	0.0079	n/a		30.38*
#2447885	Brown shrimp	Acute	0.795			0.31
#2447887	Rainbow trout	Acute	0.04			6.10*
#2447889	Bluegill sunfish	Acute	0.0058			42.07*
#2447889	amphibians	Acute	0.0058	1.3	n/a	224.14*
#2733376	*Lemna gibba G3*	7-day EC_{50}	0.0285	n/a	0.24	8.42*
#2447897	Freshwater green algae	72 hr EC_{50}	0.0045	n/a		53.33*
#2447890	Juvenile Plaice	Acute	0.06			4.07*
* indicate Level of Concern exceeded						

Table 7 Screening level risk assessment on birds and mammals

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	Risk Quotients
Small Bird (0.02 kg)				
Acute	15.50	Insectivore	158.72	10.24*
Medium Sized Bird (0.1 kg)				
Acute	15.50	Insectivore	123.87	7.99*
Large Sized Bird (1 kg)				
Acute	15.50	Herbivore (short grass)	80.01	5.16*
Small Mammal (0.015 kg)				
Acute	50.10	Insectivore	91.29	1.82*
Reproduction	10.00	Insectivore	91.29	9.13*
Medium Sized Mammal (0.035 kg)				
Acute	50.10	Herbivore (short grass)	177.06	3.53*

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	Risk Quotients
Reproduction	10.00	Herbivore (short grass)	177.06	17.71*
Large Sized Mammal (1 kg)				
Acute	50.10	Herbivore (short grass)	94.61	1.89*
Reproduction	10.00	Herbivore (short grass)	94.61	9.46*
* indicate Level of Concern exceeded				

Table 8 Refined risk assessment for aquatic species using incident data and monitoring information

Risk quotients PMRA #	Species	Type of test	Toxicity endpoint adjusted for uncertainty (mg a.i./L)	EECs (mg a.i./L)		Risk Quotients
				15 cm depth	80 cm depth	
#2447884	*Daphnia magna*	Acute	0.027	n/a	1.88E-04	0.007
#2651092	*Daphnia magna*	Chronic	0.0079	n/a		0.023
#2447885	Brown shrimp	Acute	0.795			0.0002
#2447887	Rainbow trout	Acute	0.04			0.005
#2447889	Bluegill sunfish	Acute	0.0058			0.032
#2447889	amphibians	Acute	0.0058	0.001	n/a	0.172
#2733376	*Lemna gibba G3*	7-day EC_{50}	0.0285	n/a	1.88E-04	0.007
#2447897	Freshwater green algae	72 hr EC_{50}	0.0045	n/a		0.042
#2447890	Juvenile Plaice	Acute	0.06			0.003

Table 9 **Refined risk assessment for birds using incident data, monitoring information and mean nomogram residues**

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	Risk Quotients
Small Bird (0.02 kg)				
Acute	23.20	Insectivore	0.08	0.00
Acute	23.20	Frugivore (fruit)	0.02	0.00
Dietary	15.50	Insectivore	0.08	0.01
Dietary	15.50	Granivore (grain and seeds)	0.01	0.00
Dietary	15.50	Frugivore (fruit)	0.02	0.00
Medium Sized Bird (0.1 kg)				
Acute	23.20	Insectivore	0.07	0.00
Dietary	15.50	Insectivore	0.07	0.00
Dietary	15.50	Frugivore (fruit)	0.01	0.00
Large Sized Bird (1 kg)				
Acute	23.20	Insectivore	0.02	0.00
Acute	23.20	Herbivore (short grass)	0.02	0.00
Acute	23.20	Herbivore (Broadleaf plants)	0.02	0.00
Dietary	15.50	Insectivore	0.02	0.00
Dietary	15.50	Herbivore (short grass)	0.02	0.00
Dietary	15.50	Herbivore (long grass)	0.01	0.00
Dietary	15.50	Herbivore (Broadleaf plants)	0.02	0.00

Table 10 **Refined risk assessment for mammals using incident data, monitoring information and mean nomogram residues**

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	Risk Quotients
Small Mammal (0.015 kg)				
Acute	50.10	Insectivore	0.05	0.0010
Reproduction	10.00	Insectivore	0.05	0.0048
Reproduction	10.00	Granivore (grain and seeds)	0.01	0.0005
Reproduction	10.00	Frugivore (fruit)	0.01	0.0010
Medium Sized Mammal (0.035 kg)				
Acute	50.10	Insectivore	0.04	0.0008
Acute	50.10	Herbivore (forage crops)	0.04	0.0008
Reproduction	10.00	Insectivore	0.04	0.0043

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	Risk Quotients
Reproduction	10.00	Frugivore (fruit)	0.01	0.0009
Reproduction	10.00	Herbivore (short grass)	0.05	0.0048
Reproduction	10.00	Herbivore (long grass)	0.03	0.0027
Reproduction	10.00	Herbivore (Broadleaf plants)	0.04	0.0042
Large Sized Mammal (1 kg)				
Reproduction	10.00	Insectivore	0.02	0.0023
Reproduction	10.00	Herbivore (short grass)	0.03	0.0026
Reproduction	10.00	Herbivore (long grass)	0.01	0.0015
Reproduction	10.00	Herbivore (Broadleaf plants)	0.02	0.0022

Table 11 Registered Alternative Slimicide Active Ingredients for use in Oilfield Fracturing Fluids and or Enhanced Oil Recovery Systems as of February 2018.

Active Ingredient	Registration Number for examples of an end-use product with this active ingredient
2,2-dibromo-3-nitrilopropionamide	#15506, #17573, #25107, #28994, #30326, #31222
2-(hydroxymethyl)-2-nitro-1,3-propanediol	#16821, #16822, #32054
Nabam	#18211, #18775
Alkyl-1,3-propylene diamine acetates	#19339, #20502, #26572, #32426, #33006
2-Methyl-4-isothiazolin-3-one	#19368, #29794
5-Chloro-2-methyl-4-isothiazolin-3-one	#19368, #29794
1-Alkylamino-3-aminopropane	#25340
Glutaraldehyde	#27868, #32165, #32307
Acrolein	#27928
Didecyl dimethyl ammonium chloride	#29199, #29913, #30912, #30932
N-alkyl dimethyl benzyl ammonium chloride	#24290, #25606, #32165, #32600, #33012
Sodium chlorite	#29850, #30257, #32219
Hydrogen peroxide	#32715
Sodium dimethyldithiocarbamate	#18211, #18775
Peroxyacetic acid	#32715

Table 12 List of Supported Uses

Supported label claims
Enhanced oil recovery systems and fracturing fluids at 25–130 ppm of product.

Table 13 Toxic Substances Management Policy (TSMP) Considerations – Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints	Transformation Products Endpoints
CEPA toxic or CEPA toxic equivalent	Yes		-	-
Predominantly anthropogenic	Yes		-	-
Persistence	Soil	Half-life ≥ 182 days	No data	No data
	Water Yes	Half-life ≥ 182 days	Half-life 191–371	Major transformation products are tributyl-(5-hydroxy-pentyl)-phosphonium, tributyl-(6-hydroxy-pentyl)-phosphonium and tributyl-(7-hydroxy-pentyl)-phosphonium
	Sediment Yes	Half-life ≥ 365 days	Half-life 191–371	Transformation products were not identified
	Air	Half-life ≥ 2 days or evidence of long range transport	Tributyl tetradecyl phosphonium chloride is not volatile and is not expected to volatilise from water or moist soil surfaces as vapour pressure is negligible (<5×10-06 Pa 25°C)	Transformation products were not identified
Bioaccumulation	Log $K_{ow} \geq 5$ No		Log $K_{ow} = 0$ Tributyl tetradecyl phosphonium chloride is expected be in equilibrium with organic and water phase (1:1) thus the resulting log K_{ow} would be zero.	No data
	BCF ≥ 5000		No data	Not data
	BAF ≥ 5000		No data	Not data
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No	Not data

References

A. List of Studies/Information Submitted by Registrant

PMRA Document Number	References
1.0	**Chemistry**
2453514	2004, Bellacide 350: Product Chemistry, Series 61 - Confidential Attachment, DACO: 2.11.1,2.11.2,2.11.3,2.11.4 CBI
2453515	2004, Bellacide 350: Product Chemistry, Series 62 - Confidential Attachment, DACO: 2.12.1,2.13.1,2.13.2,2.13.3 CBI
2582891	2015, Additional Starting Materials, DACO: 2.11.2 CBI
2733389	2017, Production Flow for Tributyltetradecylphosphonium chloride (CAS 81741-28-8), 50% Solution, DACO: 2.11.1,2.11.3 CBI
2733383	2017, Rationalisation of impurity formation on the TTPC Process, DACO: 2.11.4 CBI
2582892	2015, Discussion of Formation of Impurities / Impurities of human Health or Environmental Concern, DACO: 2.11.4 CBI
2641734	2016, Bellacide 350: Preliminary Analysis, DACO: 2.13.2,2.13.3,2.13.4 CBI
2733388	2017, Tributyltetradecyl Phosphonium Chloride 50% Solution: Preliminary Analysis, DACO: 2.12.1,2.13.2,2.13.3 CBI
2772856	2017, Manufacture date and location details for PSL Study 41933 and PSL study 43904 are provided, DACO: 2.13.3 CBI
2582897	2015, Preliminary Analysis - Confirmation of Identity with Proton NMR Spectrum with Assignments, DACO: 2.13.2 CBI
2453516	2004, Bellacide 350: Product Chemistry, Series 63 Self Certification and Summary of Physical. Chemical Properties, DACO: 2.14.1,2.14.10,2.14.15,2.14.2,2.14.3,2.14.4,2.14.9,830.7000 CBI
2447845	2002, Determination of Physico-Chemical Properties of DP3407 (Solid Form), DACO: 2.14.11,2.14.9 CBI
2447843	2009, Determination of Physico-Chemical Properties of DP3407 (Solid Form), DACO: 2.14.7,2.14.8 CBI
2447849	1984, Photolysis Study of Belclene 350 in water, DACO: 2.14.12 CBI
2454977	2004, 30 - Day Accelerated Stability Evaluation of Bellacide 350, DACO: 2.14.14 CBI
2733387	2017, Tributyltetradecyl Phosphonium Chloride 50% Solution: Physical and Chemical Characteristics: Color, Physical State, Odor, pH, Viscosity, and Density/relative Density, DACO: 2.14.1,2.14.15,2.14.2,2.14.3,2.14.6,830.7000 CBI
2582900	2015, TTPC TGAI Product Chemistry, DACO: 2.14,2.14.1,2.14.12,2.14.2,2.14.3 CBI
2733375	2010, DP8067: Determination of Long-Term Storage Stability and Corrosion Characteristics, DACO: 8.2.2.3

2447841 2002, Determination of some physio-chemical properties of Bellacide 350, DACO: 2.14.5,2.14.6 CBI
2582901 2015, Stability (temp, metals, sunlight), DACO: 2.14.13 CBI
2447954 2014, Chemical and Physical Properties, DACO: 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.5, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2582870 2015, Bellacide 350 Product Chemistry, DACO: 3.5.1,3.5.2,3.5.3,3.5.6,3.5.9 CBI
2733378 2017, Method Validation: Analytical Method for the Determination of Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC) in Sediment, DACO: 8.2.2.2

2.0 Human and Animal Health

2447850 1982, Acute Oral LD_{50} in the Rat, DACO: 4.2.1
2447851 1980, Acute Oral LD_{50} in the Rat of TK 12780, DACO: 4.2.1
2447852 1982, Acute Dermal LD_{50} in the Rat, DACO: 4.2.2
2447856 1980, Acute Dermal LD_{50} in the Rat of TK 12780, DACO: 4.2.2
2447857 2004, Acute Nose-Only Inhalation Toxicity Study of Bellacide 350 and Bellacide 355 in Albino Rats, DACO: 4.2.3
2447858 2004, Revised Final Report - Acute Nose-Only Inhalation Toxicity Study of Bellacide 350 and Bellacide 355 in Albino Rats, DACO: 4.2.3
2447859 1982, Eye Irritation on the Rabbit After Single Application of TK 12780/1, DACO: 4.2.4
2447860 1980, Eye Irritation on the Rabbit After Single Application of TK 12780/1, DACO: 4.2.4
2447863 1982, Skin Irritation in the Rabbit After Single Application of TK 12780/1, DACO: 4.2.5
2447864 2002, Sensitization with Bellacide 350 in Guinea Pigs (Maximization Test), DACO: 4.2.6
2447865 2007, Waiver Justifications for TTPC (CAS 81741-28-8) in Industrial Biocide Uses: Chronic Toxicity Oncogenicity Reproductive Effects Metabolism & Toxicokinetic Studies, DACO: 4.3.1,4.3.5,4.4.1,4.4.2,4.4.3,4.5.1,4.5.3,4.5.9
2447868 1983, Report on Belclene 350 (TK 12 780/2) Teratology Study in Rabbits, DACO: 4.5.2
2447871 1983, Amendment 1: Report on Belclene 350 (TK 12 780/2) Teratology Study in Rabbits, DACO: 4.5.2
2447872 1983, Salmonella/Mammalian-Microsome Mutagenicity Test, DACO: 4.5.4
2447873 1985, V79 Chinese Hamster Point Mutation Test (with and without microsomal activation), DACO: 4.5.5
2447874 1985, Nucleus Anomaly Test in Somatic Interphase Nuclei of Chinese Hamster, DACO: 4.5.7
2468934 1985, Report on Belclene 350 (TK 12780/2): Teratology Study in Rats, DACO: 4.5.2
2468938 1985, Amendment No. 1 to Final Report on Belclene 350 (TK 12780/2): Teratology Study in Rats, DACO: 4.5.2
2468939 2005, Amendment No. 2 to Report on Belclene 350 (TK 12780/2): Teratology Study in Rats, DACO: 4.5.2
2468940 2005, Amendment No. 2 to Final Report on Belclene 350 (TK 12780/2): Teratology Study in Rabbits, DACO: 4.5.2

2468942 1989, 3-Month Oral Toxicity Study in Rats (Administration in Water): Belclene 350: Final Report, DACO: 4.3.1
2468944 1987, Autoradiographic DNA Repair Test on Rat Hepatocytes (OECD-Conform), DACO: 4.5.7
2468945 1987, Autoradiographic DNA Repair Test on Human Fibroblasts (OECD-Conform), DACO: 4.5.7
2836319 2017, Study Report No. 841254; PMRA Identifier 2468942 Clarification Response on Calculations, DACO: 4.3.2 CBI
2836320 2017, rat (Study Number 82 1226; PMRA Identifier 2468934) and rabbit (Study Number 82 1227; PMRA Identifier 2447868) Historical Info, DACO: 4.5.2 CBI
2447973 2007, Occupational Exposure Assessment for TTPC (EPA), DACO: 5.1,5.2,5.3
2646615 2015, Biotransformation in Aquatic Systems, DACO: 8.2.3.5

3.0 Environment

2447878 1987, Photodegradation of Belclene 350 in Water, DACO: 8.2.3.3.2
2646618 2015, Adsorption/Desorption Properties of [14C] Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC) in Six Soils, DACO: 8.2.4.2
2646615 2015, Aerobic Aquatic Metabolism of [14C]Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC), DACO: 8.2.3.5
2733381 2015, Aerobic Aquatic Metabolism of [14C]Tri-n-Butyl Tetradecyl Phosphonium Chloride (TTPC), DACO: 8.2.3.5.4
2447894 1983, Acute Oral LD_{50} - Mallard Duck D17-516, DACO: 9.6.2.2
2447895 1983, Eight Day Dietary LC_{50} - Bobwhite Quail D17-516, DACO: 9.6.2.4
2447896 1983, Eight Day Dietary LC_{50} - Mallard Duck MLC D17-516, DACO: 9.6.2.5
2447884 1988, Report on the Test for Acute Toxicity of TK 12780/2 to Daphnia Magna, DACO: 9.3.2
2651092 2016, TTPC: A Flow-Through Life-Cycle Toxicity Test with the Cladoceran (*Daphnia magna*), DACO: 9.3.3
2447889 1983, Report on the Test for Acute Toxicity of TK 12780/2 to Bluegill, DACO: 9.5.2.2
2447887 1988, Report on the Test for Acute Toxicity of TK 12780/2 to Rainbow Trout (*Salmo gairdneri*), DACO: 9.5.2.1
2447890 1984, Belclene 350: Determination of the Acute Toxicity to Juvenile Plaice (*Pleuronectes platessa*), DACO: 9.5.2.4
2447897 2006, Determination of the effect of Bellacide 350 on the growth of fresh water green alga *Selenastrum capricornutum*, DACO: 9.8.2
2447885 1984, Belclene 350: Determination of the Acute Toxicity to Brown Shrimp (*Crangon crangon*), DACO: 9.4.2
2646612 2016, Aerobic Soil Biotransformation 20 - 30C, DACO: 8.2.3.4.2
2733376 2017, TTPC: A 7-Day Static-Renewal Toxicity Test with Duckweed (*Lemna gibba* G3), DACO: 9.8.5

4.0 Value

2447976 2014, Value Summaries, DACO: 10.1,10.2.2,10.2.3.1,10.3.1,10.3.2
2447979 2010, Biocidal Efficacy of Bellacide 350 in Fracturing Fluid, DACO: 10.2.3.2
2447983 2009, Case History 3: Waterflood System in North America, DACO: 10.2.3.3

2447985 2008, A New High Performance Quaternary Phosphonium Biocide for Microbiological Control in Oilfield Water Systems, DACO: 10.2.3.3,10.5.1
2490059 2015, Mode of Action, DACO: 10.2.1
2490060 2015, Description of Pest Problem, DACO: 10.2.2
2490061 2015, Efficacy: Laboratory Trials and Small Scale Trials Overall Summary with raw data, DACO: 10.2.3.2,10.2.3.3
2490064 2015, Efficacy: Operational Trials or Use history Information, DACO: 10.2.3.4,10.2.4
2490065 2013, TTPC Oilfield Success Story -Niobrara Well, DACO: 10.2.3.4,10.2.4,10.5.1
2490066 2015, Non-Safety Adverse Effects, DACO: 10.3.2
2490067 2015, Impact, DACO: 10.4
2490069 2015, Resistance Management, DACO: 10.5.3
2516599 2014, Biocidal Testing KemFlow A-4251Bellacide 350, DACO: 10.2.3.2(F),10.2.3.3
2516602 2004, NACE International, Standard Test Method Field Monitoring of Bacterial Growth in Oil and Gas Systems, DACO: 10.6
2516603 2010, Comparative Performance of Biocides Versus, DACO: 10.5.1,10.5.2,10.6

B. Additional Information Considered

i) Published Information

1.0 Chemistry

2.0 Human and Animal Health

2859981 Toxicology and Carcinogenesis Studies of Tetrakis(hydroxymethyl)phosphonium sulfate (THPS) and Tetrakis(hydroxymethyl)phosphonium chloride (THPC) in F344/N Rats and B6C3F1 Mice. Technical Report Series No. 296 (1987) NIH Publication No. 87-2552 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709.
2859982 2000, Toxicological Risks of Selected Flame-Retardant Chemicals. Subcommittee on Flame-Retardant Chemicals, Committee on Toxicology, Board of Environmental Studies and Toxicology, National Research Council
2859980 1999, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. World Health Organization International Agency for Research on Cancer. IARC. Lyon, France. Volume 71: Re-Evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide.
2863108 2011, ID: EPA-HQ-OPP-2011-0952-0003; Human Health Risk Assessment Scoping Document in Support of Registration Review; Oct. 31, 2011, DACO: 5.1 (https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0952-0003)

3.0 Environment

2837227 AER Compliance Dashboard – website http://www1.aer.ca/compliancedashboard/index.html

2837361 2009. Fraser, Kevin J. MacFarlane, Douglas R. Phosphonium-Based Ionic Liquids: An Overview. Aust. J. Chem. 2009, 62, 309-321. CSIRO Publishing

2830611 May 2016. Ministry of the Economy, Saskatchewan Upstream Oil and Gas IRIS Incident. Government of Saskatchewan. 1pp. http://www.publications.gov.sk.ca/details.cfm?p=78193

2741337 Kahrilas, Genevieve A.; Blotevogel, Jens; Corrin, Edward R.; and Borch, Thomas. Downhole Transformation of the Hydraulic Fracturing Fluid Biocide Glutaraldehyde: Implications for Flowback and Produced Water Quality. 2016-Sept-12. American Chemical Society. Environ. Sci. Technol. 2016, 50, 11414−11423

2837364 Notte, Chelsea Althea. Reducing Produced Water Leaks and Spills by Improving Industry Compliance in British Columbia's Natural Gas Sector. Master's of Public Policy. Simon Fraser University. Spring 2014. 97 pp.

2837366 Couling, David J., et al. Assessing the factors responsible for ionic liquid toxicity to aquatic organisms via quantitative structure-property relationship modelling. Royal Society of Chemistry, Green Chem., 2006,8, 82-90. DIO10.1039/b511333d.

2843533 05-July-2016. Directive 050: Drilling Waste Management. Alberta Energy Regulator. 167 pp. https://www.aer.ca/documents/directives/Directive050.pdf

2871884 Goss, G. et al. Unconventional Wastewater Management: A Comparative Review and Analysis of Hydraulic Fracturing Wastewater Management Practices Across Four North American Basins. University of Alberta, Canadian Water Network. Oct. 2015. 186pp.

2871886 Sang Hyun Lee and Sun Bok Lee. Octanol/water partition coefficients of ionic liquids. J Chem Technol Biotechnol 2009; 84: 202–207

2871887 Iago Rodríguez-Palmeiro, et. al. Tributyl(tetradecyl)phosphonium Chloride Ionic Liquid for Surfactant-Enhanced Oil Recovery. Energy Fuels 2017, 31, 6758-6765. American Chemical Society Publications. DOI: 0.1021/acs.energyfuels.7b00544